THE RECRUITMENT TRIANGLE: REASONS WHY AFRICAN AMERICANS ENROLL, REFUSE TO ENROLL, OR VOLUNTARILY WITHDRAW FROM A CLINICAL TRIAL

An Interim Report From the African-American Antiplatelet Stroke Prevention Study (AAASPS)

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Recruitment and retention of study subjects are key to the success of a clinical trial. In the case of minority patients, this may be challenging as minority patients have been underserved by the medical health-care system. Furthermore, minority patients are more likely to experience barriers to entry into a clinical trial such as mistrust of the medical system, economic disadvantages, lack of awareness of study programs, and communication barriers.

An open-ended questionnaire was used to determine reasons why subjects in the African-American Antiplatelet Stroke Prevention Study (AAASPS) remained in the study or voluntarily withdrew in the absence of an adverse event. Potential enrollees who refused to participate in the AAASPS also were queried. Enrollees who remained in the program consistently stated that they participated to reduce the risk of stroke recurrence and to help others by finding a "cure" for stroke. Those who withdrew or refused to participate consistently stated that they were afraid of being used as "guinea pigs."

A "recruitment triangle" emerged that might predict a patient's likelihood of participation in a clinical trial. The sides of the triangle include the patient, key family members and friends, and the primary medical doctor and other medical personnel. The organizers of a clinical trial need to be aware of the "recruitment triangle" and establish strategies to heighten and maintain its integrity. (*J Natl Med Assoc.* 1998;90:141-145.)

Key words: African Americans ◆ clinical trials ◆ recruitment

President Clinton's apology to the survivors and the family members of those who participated in the Tuskegee Study raises hope that we will move forward to dispel mistrust of the health-care system.[1-11] The apology, however, reminds us of past medical exploitation of African Americans in the form of unethical medical experimentation and other medical injustices that have led to skepticism and mistrust of the medical establishment.[12-14] In an era of medical advances and a call for participation of women and minorities in biomedical research,[15] a window of

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Table 1. Patient Characteristics

	% Group 1* (n=19)	% Group 2* (n=4)	% Group 3* (n=6)
Mean age (years)	63.8	62†	‡
Women	68	50	50
Mean education level (years)	11.9§	9.6†	‡
Household income ≥$20,000	59‖	0†	‡
Mean duration of participation in AAASPS (months)	4.7	≤1	—
Study information explained clearly	100	100†	75¶
Treated with respect by study coordinator	100	100†	100

Abbreviations: AAASPS=African-American Antiplatelet Stroke Prevention Study.
*Group 1=those who remained, Group 2=those who withdrew, and Group 3=those who refused to participate in the AAASPS.
†n=3.
‡Potential enrollees who refused to participate declined to provide this information.
§n=15.
‖n=17.
¶=4; 1 patient did not answer the question and 1 was uncertain if the information was explained clearly.

opportunity exists whereby minority health care may be advanced. If this opportunity is not embraced, health care for minorities may take a step backward.

We have had a unique opportunity to carry out a national secondary stroke prevention program–the African-American Antiplatelet Stroke Prevention Study (AAASPS). The AAASPS is a double-blind, randomized, clinical trial designed to determine the effectiveness and safety of aspirin (650 mg/day) and ticlopidine hydrochloride (500 mg/day) in the prevention of recurrent stroke, myocardial infarction, and vascular death among African-American patients with recent ischemic stroke (within 90 days).

This article reviews the reasons why AAASPS patients remained in the program, withdrew voluntarily in the absence of an adverse event, or terminated participation involuntarily. Finally, eligible study subjects who refused to participate were queried to determine why they did not enroll in the AAASPS.

METHODS

The study instrument was an open-ended questionnaire, administered by one of the authors (B.B.). Study subjects were divided into three groups: group 1 was comprised of patients who remained in the AAASPS (n=19), group 2 included those who voluntarily withdrew from AAASPS (n=4), and group 3 was comprised of patients who refused to participate in the AAASPS (n=6). The information was collected during the first 7 months of AAASPS enrollment among patients who were screened at the Rush Medical Center site. Five key content question areas were explored for each patient from each respective group:

- What were your reasons for participating (voluntarily withdrawing, refusing to participate) in the AAASPS?
- What circumstances or events may have influenced your decision to participate (withdraw, refuse to participate) in the AAASPS?
- Was the information regarding the study explained to you in words or terms that you could easily understand?
- Did the study coordinator treat you in a respectful manner?
- What was the opinion of your family members or friends regarding your being asked to participate in the AAASPS?

Information also was collected on the AAASPS enrollees' age, sex, education level, mean annual household income, and number of months that the patient had been on the study medication. Aside from the sex of the study subject, the remainder of this information was missing for those who declined to participate in the AAASPS as they refused to disclose the information. All patients who enrolled in the AAASPS gave verbal and written consent to participate in the study.

RESULTS

Group 1: Patients Who Remained in the Study

There were 19 patients in this ancillary study who

had remained in the AAASPS at the Rush Medical Center site. Mean age was 63.8 years and mean educational level was 11.9 years. Sixty-eight percent were women, and 59% had mean annual household incomes ≥$20,000. The mean duration in the study was 4.7 months, and all responded that information about AAASPS was explained in an easily understandable manner and that they were treated with respect by the AAASPS study coordinator.

When asked, 84% responded that they had participated in the study to reduce their risk of another stroke and 32% to find a "cure" for stroke or to help others. Thirty-two percent were encouraged by their physician to participate in the program, and 47% were encouraged by family or friends.

Group 2: Patients Who Withdrew From the Study

Four patients withdrew from the AAASPS at the Rush Medical Center site. Mean age was 62 years and mean educational level was 9.6 years. Fifty percent were women, and none had mean household incomes ≥$20,000. The mean duration in the study was ≤1 month, and all responded that information about the study was explained in an easily understandable manner and that they were treated with respect by the AAASPS study coordinator.

The primary reason that patients withdrew from the study was concern about being the subject of experimentation and the possibility of being a "guinea pig." When family and friends were consulted, they supported the decision to withdraw and expressed concern about government-sponsored research of blacks.

Group 3: Patients Who Refused to Participate in the Study

Six patients in this ancillary study refused to participate in the AAASPS. Fifty percent were women. Patients who refused to participate declined to furnish the interviewer with information regarding age, education, and income. Seventy-five percent indicated that study information was presented in an easily understandable manner, and all responded that they were treated with respect by the study coordinator.

Rationale for refusal to participate included concerns about experimentation, the possibility of being a "guinea pig" (33%), and other reasons (50%) that reflected concerns about changing current stroke preventative medications or other life circumstances. When family or friends were consulted, 83% reinforced the patients' concern about medical experimentation and the possibility of being a "guinea pig."

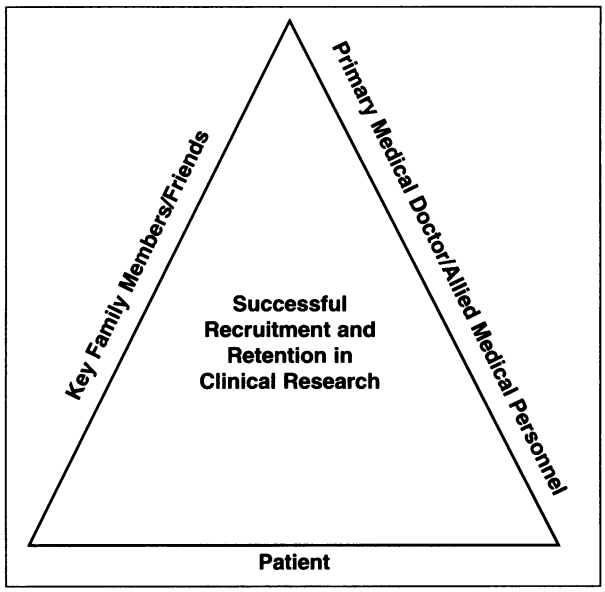

Figure.
The Recruitment Triangle.

Table 1 compares patient demographics and Table 2 lists reasons for participation, withdrawal, or refusal to participate among the three patient groups.

DISCUSSION

This study was conducted in the summer of 1996 and included patients who were screened at one of the local AAASPS sites, Rush Medical Center. Several trends were noted. First, patients who remained in the study did so to improve their health status by entering this stroke prevention program. Furthermore, about one third had altruistic goals to find a "cure" for stroke or to help others. In addition, these patients received encouragement and support to participate in AAASPS from family, or friends or their personal physician. Finally, those who withdrew or refused to participate raised concern about the nature of experimentation and the possibility of being a "guinea pig." These feelings were reinforced by the patients' family and friends.

These observations suggest that there may be a "recruitment triangle" (Figure) that is central to the enrollment and retention of patients in clinical research, especially clinical trials. The three walls of

Table 2. Reasons for Participation, Withdrawal, or Refusal and the Influence of Personal Physician, Family, or Friends

Reason	No. (%)
Group 1* (n=19)	
Personal rationale for participation	
Reduce my risk of another stroke	16 (84)
To find a cure for stroke or to help others	6 (32)
Influence of physician, family, or friends	
My personal physician encouraged me to participate	6 (32)
My family or friends encouraged me to participate	9 (47)
Group 2* (n=4)	
Personal rationale for withdrawal from study	
Concern that I am a guinea pig or being used for experimentation	4 (100)
Influence of family, friends, or others	
My family, friends, or others supported my decision to withdraw and were concerned about government research of blacks	2† (100)
Group 3* (n=6)	
Personal rationale for refusal to participate	
Concerned that I will be used as a guinea pig or for experimentation	2 (33)
Other (I do not want to change medications, I am too busy, or I might move to another state)	3 (50)
Influence of family, friends, or others	
My family, friends, or others were concerned that I might be a guinea pig or the object of an experiment	5 (83)

Abbreviations: AAASPS=African-American Antiplatelet Stroke Prevention Study.
*Group 1=those who remained, Group 2=those who withdrew, and Group 3=those who refused to participate in the AAASPS.
†n=2.

the triangle include the patient, key family members and friends, and the patient's primary medical doctor and other medical personnel. The walls are held together by social support, education about the nature of the research, and trust in study personnel and the overall program. Should one of the walls pull away from the triangle, the structure may collapse with resultant refusal to enroll in the research program or subsequent withdrawal. Thus, clinical researchers must be aware of the triangle and must strive to enlist and maintain the support of the key components of the triangle to heighten the likelihood of successful recruitment and retention of patients in clinical research.

Much has been said about the barriers to entry into a clinical research study.[1-3,7,8,16] Some of the primary barriers include mistrust, economic factors, lack of awareness about clinical research, and ineffective study staff communication. These barriers can be surmounted with careful planning.[1] Specifically, social support, education about the research, and development of trust can sever the barriers and serve as the "glue" of the "recruitment triangle." Trust may be established by using culturally sensitive study staff with good communication skills, treating the patient with respect, and taking the time to explain the research in understandable terms.

Certain patients may require more time and effort to recruit and retain in a clinical research program. Patience and sincere commitment by the study staff are important as a high-pressure approach may deter patients from the research program and engender a feeling of being treated like a "guinea pig" or an experiment. Clinical researchers must respect a patient's decision not to participate or right to withdraw from a research program.[17,18] By maintaining the integrity of the "recruitment triangle," refusal and premature voluntary withdrawal

may be minimized.

The patients who participated in this ancillary study made few direct references to the Tuskegee Syphilis Study.[14] Although the Tuskegee Syphilis Study has engendered a substantial negative image of clinical research among minorities, especially African Americans, medical exploitation, such as unethical experimentation and "night doctors,"[1,12-14] and institutional racism set the stage for mistrust of the medical system long before the infamous Tuskegee Study. Our anecdotal experience is that the Tuskegee Study has had a negative impact on AAASPS recruitment during times when the news media has given considerable coverage to the study (eg, the time period leading up to President Clinton's apology). Although a program such as the AAASPS is susceptible to the negative impact of the Tuskegee Study, the roots of mistrust of the medical system took hold well before the injustices of the latter study were unveiled. This ancillary study was carried out during a period of relatively little media attention concerning the Tuskegee Study. This may explain, at least in part, the relative lack of reference to this study among our patients.

Our results must be interpreted within the context of their limitations. Our study patients were referred and may not represent African Americans from the community at large. Furthermore, of those who remained in the AAASPS at the Rush Medical Center site and were queried as part of this ancillary study, there was nonrandom selection from among those patients who participated at the Rush site. This strategy was necessary as there were time and economic resource limitations. In addition, the number of patients in the group that withdrew and refused to participate was relatively small. Finally, there was limited demographic information on those who refused to participate in the AAASPS. This might be expected as persons who decline to enroll in a program may be less likely to share certain information, or the interviewer may have to focus his or her queries on the highest priority information in this more difficult group to access. Given the paucity of information about minority patients' rationale for enrollment, premature voluntary withdrawal, and refusal to participate in focused clinical trials, these results are important and useful if these limitations are taken into account.

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